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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/630,333 | 07/31/2000 | Anand C. Burman | U 012799-1 | 5586 |

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| EXAMINER |
|---|
| KAM, CHIH MIN |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | 16 |

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/630,333 | BURMAN ET AL. | |
| | Examiner | Art Unit | |
| | Chih-Min Kam | 1653 | |

*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED 21 April 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *14 January 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☒ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-14*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 2. NOTE: The amendment to the claims does not resolve the current issues under 35 USC 112, first and second paragraphs. It also raise new issues regarding the specific cancers recited in the claim, which require further search. In the amendment of April 21, 2003, claims 1 and 12-14 have been amended, new claims 21-51 have been added. Applicants' response and the Declaration of Dr. Rama Mukherjee have been fully considered, however, claims 12-14 and 21-51 are rejected under 35 USC 112, first and second paragraphs.

If applicants' amendment were entered, it would have the following response:

1. Claims 12-14 and 21-51 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for a composition comprising an effective amount of a peptide of the general formula I and peptides of SEQ ID NOs:3-12 having cytotoxicity in various tumor cell lines, and a method of in vitro treatment of cancer cells using the peptide, does not resonably provide enablement for treating specific cancers such as colon, lung, prostate, stomach, laryngeal, oral, breast, duodenum, ovarian or pancreatic, or leukemia or glioblastoma because the specification only indicates the cytotoxicity of the peptide for in vitro treatment (see Examples 12-14), it does not indicate the in vivo treating conditions such as the amount of the peptide administered, nor demonstrates the effects of the peptide for in vivo treatment. There are no teachings on how to extrapolate the in vitro data to in vivo treatment, and no working examples for in vivo treatment. Since the specification does not provide sufficient teachings on the treating conditions such as the dose, thus, it is necessary to carry out further experimentation to assess the effect of the peptide for in vivo treatment. In response, applicants indicate it is a common practice for testing compounds for anticancer activity in vitro on human tumor cell lines, and the Declaration of Dr. Rama Musherjee provides the in vivo data, in which SEQ ID NO:11 inhibited the growth of colon adendocarcinoma by 53% (page 8 of the response). The argument is found persuasive because the in vitro data in the specification does not provide sufficient teachings on how to obtain effective amount of the peptide required for in vivo treatment. For example, the specification indicates SEQ ID NO:11 has 19-29% cytotoxicity on PTC cell lines at concentrations 10 pM-1 uM, and it appears the cytotoxicity is not concentration dependent (see data on page 21), while in vivo data in the Declaration indicates it requires 4.25 ug/100 ul (about 40 uM) twice a day to produce antitumor activity, thus it is not apparent how to extrapolate the in vitro data to the effective amount of peptide used in vivo. Therefore, it is necessary to have further experimentation to assess the effects of these peptides.

2. Claims 13, 14 and 31-51 are rejected under 35 USC 112, second paragraph as being indefinite because the claim cites "administering effective amount", it is not clear what result is expected from administering effective amount of the peptide in the treatment of cancer.

3. Claim 51 is indefinte because the claim cites further administering a chemotherapeutic compound, however, claim 41, which claim 51 dependent from, already cites this step.

Continuation of 3. Applicant's reply has overcome the following rejection(s): If entered, the rejection of claims 1-11 under 35 USC 112, first and second paragraphs .

Continuation of 5. does NOT place the application in condition for allowance because: The amendment to the claims does not resolve current issue under 35 USC 112, first and second paragraphs for claims 12-14 and 21-51.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
May 2, 2003

Christopher S. F. Low

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SUPERVISORY PATENT EXAMINER
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